REMARKS

In the Action dated November 24, 2006, claims 68, 71, 74-76 and 76-83 are pending and under consideration. Claims 80 and 82 are objected to but would be allowable if rewritten in independent form. The Examiner states that SEQ ID NOs: 15-17 are free of prior art and SEQ ID NO: 6 remains allowed. Claims 68, 71, 74-76, 78-79, 81, 83 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. Claims 68, 71, 74, 75, 76, 78, 83 are rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enabling support. Claim 71, 75, 79, 83 are rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite. Clams 68, 71, 74-76, 78, 79, 81, 83 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by Yu et al. (*JBC*, 270(22), 13483-89, 1996).

This Response addresses each of the Examiner's objections and rejections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

In the first instance, Applicants, through the undersigned, wish to thank Examiner Maryam Monshipouri for the courtesy and assistance extended to Applicants during a telephone interview on March 7, 2007. During the interview, the Examiner agreed that the outstanding Action should have been issued as a non-final Action.

In an effort to favorably advance prosecution, Applicants have amended Claims 68, 71, 74-76 and 78 to delete the recitation "or a fragment thereof," without prejudice. Applicants reserve the right to pursue the fragments of the claimed isolated proteinaceous molecules in a continuation application. Applicants have also amended Claims 68 and 74 to clarify that the stringency conditions are "high" stringency conditions. Support for such amendment is found in the specification, e.g., at page 17, lines 12-15. Claims 68 and 74 have

also been amended to recite specific high stringency wash conditions of 0.1×SCC, 0.5% w/v SDS at 60°C, which finds support in the specification, e.g., at page 47, line 26. Additionally, Claims 68 and 74 have been amended to correct the spelling of the term "complementary" and to delete references to the term "about." Applicants have also added Claim 84-85, which recite a hybridization temperature of 65°C, as suggested by the Examiner during the telephone interview. Support for the high stringency hybridization temperature of 65°C is found in the specification, e.g., at page 47, line 25 and any textbook of molecular biology, e.g., *Molecular Cloning*, Cold Spring Harbor Laboratory Press, 1982. No new matter is introduced by the amendment to Claims 68, 71, 74-76 and 78 or the addition of Claims 84-85. In addition, Applicants have also canceled Claims 79-83, without prejudice.

Claims 68, 71, 74-76, 78-79, 81, and 83 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner contends that the present application only describes a single species of the claimed genus. In addition, the Examiner alleges that even though specific parameters of the hybridization conditions are recited, the claims are still too broad to satisfy the written description requirement. The Examiner further alleges that that the recitation of "fragments thereof" lacks descriptive support.

Applicants respectfully submit that 68, 71, 74-76, 78, as amended, recite high stringency hybridization conditions and no longer recite the phrase "fragments thereof." Applicants submit that it is well recognized in the art that the higher the stringency of the wash conditions, the higher the degree of complementarity will be between hybridized sequences. In this regard, Applicants submit **Exhibit A**, which is an excerpt of Maniatis et al. (*Molecular Cloning: A Laboratory Manual.* Cold Spring Harbor Laboratory Press, Cold Spring Harbor,

N.Y., 1982). Exhibit A states that hybridizations can be performed at 42°C in 50% formamide (see page 324) and that washing conditions should be as stringent as possible (see page 325), presumably to ensure a high degree of complementarity between the hybridized sequences. Accordingly, Applicants submit that 68, 71, 74-76, 78, as amended, are sufficiently supported by the disclosure of the present application, which conveys to one skilled in the art that the inventor had possession of the claimed subject matter at the time of the filing of the application. The rejection with respect to Claims 79, 81 and 83 is moot in view of cancellation of these claims.

Therefore, Applicants respectfully submit that the written description rejection of Claims 68, 71, 74-76, 78-79, 81, 83 under 35 U.S.C. 112, first paragraph, is overcome. Withdrawal of the rejection is respectfully requested.

Claims 68, 71, 74, 75, 76, 78, 83 are rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enabling support. The Examiner acknowledges that the specification enables isolated polypeptides encoded by SEQ ID NO: 5. However, the Examiner alleges that the specification does not provide enablement for fragments of the expression products or fragments of the variants of the expression products with no proteins activity. The Examiner alleges that the specification fails to teach which residues in claimed fragments is in charge of assigning function to SEQ ID NO:6 fragments or variant of SEQ ID NO:6 fragments. The Examiner contends that current state of the art indicates that many fragments of a full-length polypeptide are totally incapable of retaining any function corresponding to the full-length polypeptide.

Applicants respectfully submit that Claims 68, 71, 74, 75, 76, 78, as amended, no longer recite the phrase "fragments thereof." Applicants also submit that Claim 83 has been canceled, without prejudice. Therefore, Applicants respectfully submit that the of Claims 68, 71,

74, 75, 76, 78, 83 under 35 U.S.C. 112, first paragraph, as allegedly lacking enabling support is moot and withdrawal thereof is respectfully requested.

Claim 71, 75, 79, 83 are rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite. The Examiner contends that it is unclear as to how both a full-length proteinaceous molecule and fragments thereof are set forth by a single amino acid sequence.

Applicants respectfully submit that Claims 71 and 75, as amended, no longer recite the phrase "fragments thereof." Applicants also submit that Claims 79 and 83 have been canceled, without prejudice. Therefore, Applicants respectfully submit that the rejection of Claims 71, 75, 79, 83 under 35 U.S.C. 112, second paragraph, is overcome and withdrawal thereof is respectfully requested.

Clams 68, 71, 74-76, 78, 79, 81, 83 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by Yu et al. (*JBC*, 270(22), 13483-89, 1996). The Examiner alleges that Yu et al. disclose a polypeptide having serine proteinease activity, the sequence of which has 33.5% homology to residues 6-313 of SEQ ID NO:6 and can be considered to be fragment of SEQ ID NO:6 encoded by a sequence hybridizing to SEQ ID NO:5 of this invention under stringent conditions recited in Claim 68, thereby anticipating Claims 68, 71-78-79. The Examiner also alleges that Yu et al. teach about a human plasma (which can be considered to be a pharmaceutically acceptable carrier) comprising its wild type proteinase, wherein said proetinase by inherency is glycosylated, thereby anticipating Claims 74, 76, 81 and 83. The Examiner further alleges that Yu et al. teaches the expression product of its full-length cDNA, as well as reducing and non-reducing buffers comprising the expression product, which anticipates Claim 75.

Applicants submit that Claims 79, 81 and 83 have been canceled, without prejudice. With respect to Claims 68, 71, 74-76, 78, Applicants submit that the claims, as amended, no longer recite "fragments thereof." Additionally, Applicants respectfully submit that the high stringency conditions now defined in the claims, as amended, would exclude the allegedly 33% homologous sequence disclosed by Yu et al. from the claimed molecules, thereby rendering the Examiner's rejection moot.

Therefore, Applicants respectfully submit that the rejection of Clams 68, 71, 74-76, 78, 79, 81, 83 under 35 U.S.C. 102(b) as allegedly anticipated by Yu et al. is moot or overcome in view of the amendment to Claims 68, 71, 74-76 and 78 and the cancellation of Claims 79, 81 and 83. Withdrawal of the rejection is respectfully requeseted.

Claims 80 and 82 are objected to for depending upon a rejected base claim. In view of cancellation Claims 80 and 82, the objection is moot and withdrawal thereof is respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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Encl: Exhibit A

HYBRIDIZATION OF DNA OR RNA IMMOBILIZED ON FILTERS TO RADIOACTIVE PROBES

There are many methods available to hybridize radioactive probes in solution to DNA or RNA immobilized on nitrocellulose filters. These methods differ in the following aspects:

- the solvent and temperature used (68°C in aqueous solution or 42°C in 50% formamide);
- the volume of solvent and the length of hybridization (large volumes for periods as long as 3 days or minimal volumes for times as short as 4 hours);
- the degree and method of agitation (continuous shaking or stationary);
- the concentration of the labeled probe and its specific activity;
- the use of compounds, such as dextran sulfate, that increase the rate of reassociation of nucleic acids;
- the stringency of washing following the hybridization.

Although the choice depends to a large extent on personal preference, we would like to offer the following guidelines.

1. Hybridization reactions in 50% formamide at 42°C are easier to set up, present less of an evaporation problem, and are less harsh on the filters than is hybridization at 68°C in an aqueous solution. The kinetics of the hybridization reaction in 80% formamide are approximately three to four times slower than in an aqueous solution (Casey and Davidson 1977). Assuming a linear relationship between the rate of hybridization and formamide concentration, the rate in 50% formamide should be two times slower than in an aqueous solution.

2. The smaller the volume of hybridization solvent, the better. The kinetics of nucleic acid reassociation are faster, and the amount of probe needed may be reduced so that the DNA on the filter acts as the driver for the reaction. All these are important parameters when detecting clones of low-abundance mRNAs. However, it is essential that sufficient liquid be present for the filters to remain at all times covered by a film of the hybridization solution.

3. Continual movement of the probe solution across the filter is unnecessary, even for a reaction driven by DNA immobilized on the filter. However, if a large number of filters are hybridized simultaneously, agitation is advisable in order to prevent the filters from adhering to each other.

4. The kinetics of the hybridization reaction are difficult to predict from theoretical considerations, partly because the exact concentration of the immobilized nucleic acid and its availability for hybridization are unknown.

When using probes made by nick translation of double-stranded DNA, the following rule of thumb is useful: Allow the hybridization to proceed for a time sufficient to enable the probe in solution to achieve 1-3× $C_0t_{1/2}$. In 10 ml of hybridization solution, 1 μg of a probe of 5-kb complexity will reach $C_0t_{1/2}$ in 2 hours. To determine the time of half-renaturation for any other probe, simply enter the appropriate values into the following equation:

$$\frac{1}{X} \times \frac{Y}{5} \times \frac{Z}{10} \times 2 = \text{number of hours to achieve } C_0t_{1/2}$$

where,

X = the weight of probe added (in μg)
Y = its complexity (for most probes, complexity is proportional to the length of the probe in kb)
Z = the volume of the reaction (in ml)

After hybridization for 3× $C_0t_{1/2}$ has been reached, the amount of the probe available for additional hybridization to the filter is negligible. For single-stranded cDNA probes, the hybridization time may be shortened since the lack of a competing DNA strand in solution favors hybridization to DNA bound to the filter.

5. In the presence of dextran sulfate, the rate of association of nucleic acids is accelerated because the nucleic acids are excluded from the volume of the solution occupied by the polymer. Their effective concentration is therefore increased. The rate of association reportedly increases 10-fold in the presence of 10% dextran sulfate (Wahl et al. 1979).
   Although dextran sulfate is useful in circumstances where the rate of hybridization is the limiting factor in detecting sequences of interest, it is unnecessary for most purposes. It is also difficult to handle because of its viscosity and sometimes can lead to high backgrounds.

6. In general, the washing conditions should be as stringent as possible; i.e., a combination of temperature and salt concentration should be chosen that is slightly (5°C) below the T_m of the hybrid under study. The temperature and salt conditions can often be determined empirically in preliminary experiments where Southern blots (see pages 382ff) of genomic DNA are hybridized to the probe of interest and then washed under conditions of different stringency.